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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,168	02/26/2002	Chen W. Liaw	AREN-0320	6169

35133 7590 07/25/2005

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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,168	LIAW ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-50* is/are pending in the application.

4a) Of the above claim(s) *45-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37 and 40-44* is/are rejected.

7)☒ Claim(s) *38 and 39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/22/05 5/29/02*. 12/22/03 PTO
4) ☒ Interview Summary (PTO-413), interview date 5/20/05 Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Response to Restriction requirement filed 4/8/05 has been entered. Amendment filed 3/3/0/05 has been entered. IDS 5/29/2 has been considered.

Election/Restriction

2. Applicant's election with traverse of Group I (Claims 37-44) drawn to polynucleotide and means of expression on 4/28/05 is acknowledged. The traversal is on the ground(s) that it has not been established that there is a serious burden on the Examiner and that a search of the databases may easily facilitate the identification of the corresponding polypeptide and vice versa. Applicant's arguments have been fully considered but are not found persuasive. A search of groups I-V would not be co-extensive particularly with regard to the literature search. An examination of the materially, structurally, functionally different and patentably distinct inventions in a single application would constitute a serious undue burden on the examiner.

In a telephone interview with Quan L. Nguyen on 5/20/05, Applicants Attorney, was informed that the response to restriction requirement filed 4/28/05 was not fully responsive to the prior office action because applicant did not elect a single polynucleotide or polypeptide sequence as required by the restriction mailed by the Office on 3/20/05 (see bottom of page 5 of the Restriction Requirement). The restriction requirement stated:

"In addition to the restriction requirement above, an additional restriction requirement is imposed. Applicant is required to elect a single polynucleotide or polypeptide sequence, as appropriate, as well as one of the groups specified

above. These sequences are distinct, each from the other. They differ in sequence and therefore in structure and thus are patentably distinct. Further, each requires separate searches of the database. Thus to search all of the claimed sequences would impose an undue burden."

Quan L. Nguyen elected SEQ ID NO: 16, 84 and 85 on 5/20/05 for further prosecution. Applicant in responding to this Office action must make affirmation of this election.

Applicant is reminded that upon the cancellation of claims to a non-elected Invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Therefore, Group I (Claims 37-44) drawn to polynucleotide encoding the non-endogenous, constitutively activated version of the wild type G protein-coupled receptor (GPCR) of SEQ ID NO: 16 will be examined. Also examined will be the polynucleotide (SEQ ID NO:85) encoding the non-endogenous, constitutively activated GPCR (SEQ ID NO:84), which is the constitutively activated version of the wild type G protein-coupled receptor of SEQ ID NO: 16

Applicant is required to cancel/amend elected claims pertaining to non-elected invention, i.e. relating to non-elected polynucleotides and polypeptides.

Priority given to some parent cases but not others:

3. According to the priority statement of 2/26/02, it appears that the claimed subject matter defined in the instant application is not supported by the parent applications. Based on the information given by applicant and an inspection of the patent applications, the examiner has concluded that the subject matter defined in this application is supported by the disclosure in instant application serial no. 10/083,168, filed 2/216/02, but is not supported by any of the others because the utility for claimed invention is not supported by the parent applications. At the time of filing of instant invention GPR35 was known as an orphan receptor (endogenous ligand was unknown, see O'Dowd et al., 47 (2), Genomics 310, 1998). GPR35 had no known function. The utility of GPR35 and the constitutively activated version of GPR35 resides in its ability to interact with transcription factor E2F, which is necessary for initiating DNA replication and ultimately, cell proliferation, said utility only being disclosed in instant application and not in parent applications. Further, the constitutively activated versions of GPR35 disclosed in SEQ ID NO: 84 and 85 are only disclosed in instant application and not in parent applications. Accordingly, the subject matter defined in claims 37-44 has an effective filing date of 2/26/02.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 2/26/02 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 2/26/02.

Specification

4. The disclosure is objected to because of the following informalities:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78) as well as the relationship of instant application to the parent. Parent application 09/170,496 issued as Patent 6,555,339 and must be indicated as such.

Appropriate correction is required.

Sequence Rules Compliance

5. This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Figure 20A and 20B must be identified by their corresponding SEQ ID NO:. Compliance with sequence rules is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37 and 40-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 37, the phrase "constitutively activated version of a wild type" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "version"), thereby rendering the scope of the claim(s) unascertainable. The specification discloses that a constitutively activated receptor means a receptor subjected to constitutive receptor activation. The limitation of the wild type receptor is contained in the claims (defined sequence). It is not clear what percent sequence identity of the constitutively activated receptor to the wild type renders it a constitutively activated "version" of that receptor. For example if the constitutively activated receptor contains ten amino acids that are identical to the wild type is it a constitutively activated version of the wild type? If the constitutively activated receptor contains 200 amino acids that are identical to the wild type is it a constitutively activated version of the wild type? It is suggested to overcome the rejection the claim be amended to include a specific method by which the wild type G-protein coupled receptor (GPCR) is mutated to obtain the constitutively activated version. In this manner the number of mutations will be limited to certain regions of the receptor and thus provide clear structural limitations by which the scope of the receptor can be identified.

Claims 40 and 41 are indefinite because it is not clear what is the difference between an expression vector (claim 41) and a vector (claim 40) so as to allow the metes and bounds of the claims to be defined. The specification does not provide a clear distinction between expression vector and vector.

Claims 38-39 and 42-44 are objected for depending on an indefinite base claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37, 40-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Dowd et al (see IDS, Genomics Vol. 47 (2), 15 January 1998, pages 310-313) or Polonsky et al (US Patent 6235481) as applied to claims 37-40-44 above, and further in view of Samama et al (see IDS, J. Biol.

Chem, Vol 268 (7), 1993, pages 4625-4636) and Pauwels et al (see IDS, Molecular Neurobiology, Vol. 17, 1998, pages 109-135.

O'Dowd discloses an isolated polynucleotide encoding a GPR35 (wild type GPCR) which has 99.6% query match and 99.7% best local similarity to he GPCR of SEQ ID NO: 16. O'Dowd also discloses the molecular cloning, tissue distribution and chromosomal localization of the GPR35. In addition, O'Dowd states that further experiments will attempt to determine the endogenous ligands that bind to the receptor, which will help to elucidate its physiological role. Both the specification (page 38) and O'Dowd refer to the same GPCR, GPR35, but there appears to a one amino acid difference in the sequence of the receptor. Absent evidence to contrary the Examiner believes the GPR35 (wild type) receptor of both disclosures is the same and the differences are due to sequencing error. O'Dowd does not disclose the production of constitutively activated GPCRs.

Polonsky discloses an isolated polynucleotide encoding a wild type GPCR which has 100% query match and 100% best local similarity to he GPCR of SEQ ID NO: 16. Polonsky also discloses the molecular cloning of said receptor. Polonsky does not disclose the production of constitutively activated GPCRs.

Samama discloses the production and isolation of constitutively activated G-protein coupled receptors using sequence identity data (see Experimental Procedures). Samama also discloses the construction of constitutively activated GPCR mutant cDNA, vectors containing said GPCR, transfection of cells with said vector, host cells transfected with said vector, isolation of membranes from

said cells, and methods of assaying the activity of the constitutively activated GPCR. Samama produced the constitutively activated GPCRs to study the pharmacological and biochemical behavior of these receptors, test whether the properties of the mutants could be accommodated by the "Ternary complex Model", and study the effects of agonists and antagonists on the receptor. Samama specifically states, "Constitutively active receptor mutants should thus provide valuable means of studying the molecular properties of activated receptors and the mechanism which regulates their formation. Following the large scale production and purification of mutant receptor molecules, *in vitro*, reconstituted systems should permit a closer assessment of their molecular properties", see page 4635, column 2, fourth paragraph.

Pauwels discloses the production of constitutively activated GPCRs using sequence identity data and the effects of agonists and antagonists on their activity. The review article discloses that production of constitutively activated GPCRs is routine in the art.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use the GPCRs taught by O'Dowd or Polonsky to make polynucleotide constructs which are constitutively activated GPCRs by using the teaching of Samama and Pauwels for use in vectors, productions of transfected host cells which could be used to determine the endogenous ligands that bind to the receptor, which will help to elucidate its physiological role. Similarly the membranes form the transfected host cell containing the constitutively activated GPCRs could be used in ligand binding

assays as disclosed by Samama (page 4626). The ordinary artisan would have been motivated to modify GPCRs taught by O'Dowd or Polonsky to make polynucleotide constructs which are constitutively activated GPCRs because as stated by Samama, "Following the large scale production and purification of mutant receptor molecules, *in vitro*, reconstituted systems should permit a closer assessment of their molecular properties",

The ordinary artisan would have expected success at producing the constitutively activated GPCRs because such methods were well known in the art.

8. Claims 38 and 39 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on 571272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nirmal S. Basi
Art Unit 1646
June 30, 2005

JOSEPH MURPHY
PATENT EXAMINER